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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,270	05/02/2006	James A. Baum	38-21(52806)B	4307

27161 7590 05/06/2011

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
05/06/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,270	BAUM ET AL.	
	Examiner	Art Unit	
	ANNE KUBELIK	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,14,18-21,27,35,36 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,14,18-21,27,35,36 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/24/2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-8, 14, 18-21, 27, 35-36 and 48 are pending.

2. Applicant again argues the restriction, which was made FINAL in the Office action mailed 27 May 2009.

Applicant urges that the sequences encode insecticidal proteins with a high degree of similarity, that are secreted using an amino terminal targeting sequence and are insecticidal to coleopterans; tIC851 does not have these features (Reply to Written Opinion pg 3).

This is not found persuasive because none of these features were required by the claims; further, instant claims 6, 7, 14, 21 and 27 specifically omit the amino terminal targeting sequence. Further, no protest was filed in PCT/US04/21692 within one month of the mailing of the lack of unity (*i.e.*, within one month of 3 June 2005). Unity of Invention is not argued in response to a Written Opinion. The restriction remains FINAL.

3. Applicant is reminded that under 37 CRF 121, a clean copy of the amended claims is not to be submitted.

4. The objection to claims 2-5, 7-8, 14, 21, 27 and 35 because of informalities is withdrawn in light of Applicant's amendment of the claims.

5. The rejection of claims 1-5, 14 and 21-22 under 35 U.S.C. 103(a) as being unpatentable over Blenk et al (1996, US Patent 5,573,766) in view of Donovan et al (1988, Mol. Gen. Genet. 214:365-372), further in view of Donovan (1991, US Patent 5,024,837) is withdrawn in light of Applicant's arguments and the response to the Request for Information filed 16 March 2010.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-8, 14, 18-21, 27 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 27 May 2009, as applied to claims 1-5, 14 and 21-22. Applicant's arguments filed 24 November 2009 have been fully considered but they are not persuasive.

The full scope of toxin-encoding nucleic acids from Bacillus species are not described

Claims 1-4, 14, and 48 require nucleic acids encoding *Bacillus* toxins, wherein the nucleic acids encodes an insecticidal toxin "substantially as set forth in SEQ ID NO:6. Claims 6-8 and 18-20 require nucleic acids encoding *Bacillus* toxins, wherein the nucleic acids encodes an insecticidal toxin "substantially as set forth" in "amino acids 44-365" [*sic*, see 112, 2nd, rejection below] of SEQ ID NO:6. Claims 27 and 35-36 require a nucleic acid encoding *Bacillus* toxins that have 78% identity to SEQ ID NO:6.

The specification does not describe the structural features that distinguish toxins from *Bacillus* from toxins or other proteins from other sources, including manmade toxins and proteins. The specification does not the structural features that distinguish toxins from *B.*

thuriengiensis, B. sphaericus or *B. laterosperous* from toxins or other proteins from other *Bacillus* species.

The only species described in the specification encode SEQ ID NO:6, 4, 8, 10 and 33; the latter four have 91.1%, 82.4%, 83.1% and 82.0% identity to amino acids 44-364 of SEQ ID NO:6, respectively. No species has 78% identity to amino acids 44-364 of SEQ ID NO:6.

Further, all these species are from a single *Bacillus* species, *B. thuringiensis*. The specification does not describe any sequences from other *Bacillus* species.

Thus, the specification does not describe nucleic acids within the full scope of the claims.

The full scope of nucleic acids encoding toxins with 78% identity to SEQ ID NO:6 or a variant of it are not described

Claim 21 requires nucleic acids encoding *Bacillus* toxins that have 78% identity to "amino acids 44-365" [*sic*, see 112, 2nd, rejection below] of SEQ ID NO:6 or a variant thereof.

As discussed above, the specification fails to describe any structural features required for toxicity. Further, neither the specification nor the prior art describe the necessary and sufficient structural elements of a toxin.

Variant proteins are defined in the specification (pg 26, lines 13-40) as follows:

> With reference to the proteins of the instant application, the terms "variant amino acid sequence", or "amino acid sequence variant", or "modified amino acid sequence variant" are intended to refer to amino acid sequences that are substantially equivalent to the amino acid sequences of the present invention ....
>
> Proteins that are substantially equivalent to the proteins of the instant application are intended to be biologically functionally equivalent. As used herein, the phrase "biological functional equivalents", with respect to the insecticidal proteins of the present invention, are peptides, polypeptides and proteins that contain a sequence or moiety exhibiting sequence similarity to the novel peptides of the present invention ... and that exhibit the same or similar functional properties as that of the polypeptides disclosed herein, including insecticidal activity.

Thus, it appears that any toxin would be a variant of SEQ ID NO:6.

Thus, the specification does not describe the full scope of toxins, and does not describe the full scope of these claims.

Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO:6, 4, 8, 10 and 33 are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described nucleic acids within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, Applicant does not appear to have been in possession of the claimed genus at the time this application was filed.

Response to Arguments

Applicant urges that Applicants are not required to disclose all species encompassed by their claims and that they must merely teach those of ordinary skill in the art how to make and use those species with the disclosed utility, citing In re Vaeck (response pg 3).

This is not found persuasive because teachings how to make and use are matters under enablement, not written description.

There is no requirement in this rejection that all species encompassed by the claims be disclosed.

Applicant urges that they have taught one of skill in the art to identify sequences from Bacillus species that have the properties of SEQ ID NO:4, 6, 8, 10 and 33; one of skill in the art

could use the teachings of the specification to find other members of the genus, including those encoding an N-terminal sequence for secretion (response pg 4).

This is not found persuasive. A teaching of how to find other members of the genus may meet the requirement under enablement; however, this is not a rejection under enablement. The claims are rejected under written description.

Applicant urges that the examiner is overlooking the requirement that the sequences exhibit substantial equivalence to SEQ ID NO:6, are secreted from Bacillus species and have insecticidal activity consistent with that of SEQ ID NO:6 (response pg 4-5).

This is not found persuasive. There is no requirement in the definition of substantially equivalent that the proteins have all the properties of SEQ ID NO:6. Thus, the proteins are not required to be secreted or have the same insecticidal activity as SEQ ID NO:6. Further, the specification has not described the structural features that confer this claimed function, nor have any species from any Bacillus species other than B. thuringiensis been described.

See *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, 94 USPQ2d 1161 (Fed. Cir. 2010) at pg 1171:

> For example, a generic claim may define the boundaries of a vast genus of chemical compounds, and yet the question may still remain whether the specification, including original claim language, demonstrates that the applicant has invented species sufficient to support a claim to a genus. The problem is especially acute with genus claims that use functional language to define the boundaries of a claimed genus. In such a case, the functional claim may simply claim a desired result, and may do so without describing species that achieve that result. But the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus…
>
> [M]erely drawing a fence around the outer limits of purposed genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-8, 14, 18-21, 27, 35-36 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 27 May 2009, as applied to claims 14, 21-22, 27 and 35-36. Applicant's arguments filed 24 November 2009 have been fully considered but they are not persuasive.

Claim 14 does not set forth any steps involved in the method/process; it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. It is noted that everything in the claim is preamble.

Claim 21 is indefinite in its recitation of "said toxin protein comprises a sequence that exhibits at least about 78% sequence identity to the amino acid sequences of ... a coleopteran toxin variant [of SEQ ID NO:6]". 78% identity to a variant of SEQ ID NO:6 is indefinite as the specification does not define "variant"; thus, the polynucleotide does not have 78% identity to a fixed reference sequence. Thus, the metes and bounds of the claim are unclear.

Claims 21 and 27 are indefinite in their recitation of "at least about 78% identical". There is nothing in the specification to provide any indication as to what range of specific identity is covered by the term "about." Thus, the minimum number implies by "at least" in unclear, and the metes and bounds of the claim are unclear.

The following rejections are new and due to Applicant's amendment of the claims:

Claims 1 and 14 are indefinite in their recitation of "substantially as set forth in SEQ ID NO:6", and claims 6-7 are indefinite in their recitation of "substantially the amino acid sequence as set forth in SEQ ID NO:6". It is not clear how different a sequence must be from SEQ ID NO:6 to not be "substantially" SEQ ID NO:6. The recitation in claim 48 that the sequence is from any of three species and the recitation in claim 14 that the protein is encoded by a nucleic acid that hybridizes to any of 7 nucleic acid sequences, some of which encode proteins with less than 80% identity to SEQ ID NO:6, suggests a great deal of difference in sequence from SEQ ID NO:6 is encompassed by the phrase. As the metes and bounds of the claims are unclear, for purposes of examination, the term is interpreted as meaning any level of identity to SEQ ID NO:6.

Claims 6, 7, 14, 21 and 27 are indefinite in their recitation of "SEQ ID NO:6 from amino acid position 44-365" as SEQ ID NO:6 is only 364 amino acids long.

Response to Arguments

Applicant urges that the rejections are overcome by the amendments to the claims (response pg 5).

This is not found persuasive because they are either not so overcome or no amendments were made that addressed the rejections.

Claim Rejections - 35 USC §§ 102, 103

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-4, 14, 21 and 48 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Brown et al (1994, US Patent 5,308,760). Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 27 May 2009, as applied to claims 1, 5, 14 and 21-22. Applicant's arguments filed 24 November 2009 have been fully considered but they are not persuasive.

Brown et al teach isolation of a *B. thuringiensis* gene encoding a *Manduca sexta* toxin and the cloning of the gene into a recombinant DNA construct (column 8, line 25, to column 11, line 11). The sequences taught by Brown et al would hybridize to SEQ ID NO:5 under "stringent hybridization conditions".

Alternately, if the sequences taught by Brown et al do not hybridize to SEQ ID NO:5 under "stringent hybridization conditions", then the proteins taught by Brown et al makes obvious all nucleic acids that encode them, as the protein has a region with a high degree of identity to SEQ ID NO:6:

```
Qy        124 QMG-LKIEA--LNDMDVTNIDYTSKTGDTIYNGISELTNYTGTTQKMKTDSFQRDYTKSE 180
              |:| :::|   ||   |  :|::      ::|  |         |: :| ||    |::
Db         38 QIGNIEVEPGNLNFSVVPELDFS--VSQDLFNNTS--------VQQSQTASFNESRTETT 87

Qy        181 STSVTNGLQLGFKVA------AKGVVALAGADFETSVT--YNLSSTTTETNTISDKFTVP 232
              ||:||:|:: |  |:      || :|        |:|:  || ||||| |||::  :::
```

```
Db        88 STAVTHGVKSGVTVSASAKFNAKILVKSIEQTITTTVSTEYNFSSTTTRTNTVTRGWSI- 146

Qy       233 SQEVTLSPGHKA-----VVKHD------LRKMVYFGTHDLKGDLKVGFNDKEIVQKFIYP 281
             :| | : |  :       : | |      |   ||  |  | |:               |
Db       147 AQPVLVPPHSRVTATLQIYKGDFTVPVLLSLRVYGQTGTLAGN----------------P 190

Qy       282 NYRSIDLSDIRKTMIEIDKWNHVNTIDFYQLVGVKNHIK-----NGDTLYIDTPAEFTFN 336
             :: |:  :    |:                |  :: ||          ||         |
Db       191 SFPSLYAATYENTL----------------LGRIREHIAPPALFRASNAYIS-------N 227

Qy       337 GANPYYRATFT 347
             |    :| | |
Db       228 GVQAIWRGTAT 238
```

Nucleic acids encoding this region would hybridize to SEQ ID NO:5 under "stringent hybridization conditions". The protein is "substantially as set forth in SEQ ID NO:6".

Response to Arguments

Applicant urges that the rejections are overcome by the amendments to the claims (response pg 5).

This is not found persuasive because the amendments make the claims even more indefinite (See 112, 2nd, rejection above).

Claim Rejections - 35 USC § 103

13. Claims 1-4, 6-8, 14, 18, 20-21 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al (1994, US Patent 5,308,760) in view of Barton et al (1997, US Patent 5,608,142).

The claims are drawn to a "modified" polynucleotide encoding a protein "substantially as set forth in SEQ ID NO:6" and host cells, including cotton cells, transformed with it.

The teachings of Brown et al are discussed above. Brown et al do not teach expressing the gene in a plant.

Barton et al teach expressing of a *Manduca sexta* toxin in cotton (claims 1-4).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to express the protein taught by Brown et al in cotton, as described in Barton et al. One of ordinary skill in the art would have been motivated to do so because substitution of one *Manduca sexta* toxin for another is an obvious design choice.

14. Claim 5 is free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid of SEQ ID NO:5. Claim 27 and 35-36 are free of the prior art given the failure of the prior art to teach or suggest an isolated nucleic acid encoding a protein with 78% identity to SEQ ID NO:6. Claim 19 is free of the prior art, given the failure of the prior art to teach or suggest expressing a *Manduca sexta* toxin in a monocot.

15. Claim 5 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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May 5, 2011

/Anne R Kubelik/
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